



FDA Alert for Healthcare Professionals

Isotretinoin (marketed as Accutane)

FDA ALERT [05/2005]: FDA continues to assess reports of suicide or suicide attempts associated with the use of isotretinoin. Isotretinoin may be linked to depression and more rarely other psychiatric disorders. In some cases, the psychiatric illness is severe and there have been suicide attempts and suicides. Although causality has not been established for these reports, awareness of signs and symptoms is important. All patients treated with isotretinoin should be observed closely for symptoms of depression or suicidal thoughts, such as sad mood, irritability, anger, loss of pleasure or interest in social or sports activities, sleeping too much or too little, changes in weight or appetite, school or work performance going down, or trouble concentrating.

This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of Accutane, please contact the FDA MedWatch program at 1-800-FDA-1088 or <http://www.fda.gov/medwatch/report/hcp.htm>

Recommendations

- All patients treated with isotretinoin should be observed closely for symptoms of depression or suicidal thoughts and referred to a specialist if necessary.
- All patients should be informed to discontinue isotretinoin, and inform his/her healthcare professional right away if any of the following happens:
 - Start to feel sad or have crying spells
 - Lose interest in activities once enjoyed
 - Sleep too much or have trouble sleeping
 - Become more irritable, angry, or aggressive than usual (for example, temper outbursts, thoughts of violence)
 - Have a change in appetite or body weight
 - Have trouble concentrating
 - Withdraw from family or friends
 - Experience loss of energy
 - Experience feelings of worthlessness or inappropriate guilt
 - Start having thoughts of self-harm, or suicide
- Discontinuation of the drug may not be sufficient; psychiatric evaluation and further intervention may be necessary.

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*Report serious adverse events to FDA's MedWatch at 1-800-FDA-1088; or www.fda.gov/medwatch/report/hcp.htm
Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
Druginfo@cder.fda.gov*



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- Physicians are reminded that isotretinoin is marketed with a risk management plan to reduce fetal exposure to the drug. The goals of the program are that ***no woman should be given isotretinoin if she is pregnant and that no pregnancy should occur while a woman is taking isotretinoin.***

Data Summary

Some of the serious adverse event reports FDA has received regarding isotretinoin include birth defects and psychiatric effects (i.e., suicide ideation and suicide). Isotretinoin is a well established teratogen. Although causality has not been established for isotretinoin and psychiatric events, the following information is important to consider:

- Preclinical and neuroimaging data suggest that isotretinoin produces behavioral effects (i.e. activation) in rats, impairment of neuronal division in the murine hippocampus, and reductions in orbitofrontal brain metabolic rates in humans. This preclinical and neuroimaging data may suggest biological plausibility for the suspected psychiatric adverse events associated with isotretinoin.
- From isotretinoin's initial marketing in 1982 through August 2004, 4,992 spontaneous reports of psychiatric disturbances associated with using isotretinoin in patients in the United States have been submitted to the FDA.
- The number of reported suicides among isotretinoin users in the United States was 190 through January 2005. Between 1982 and 2002, there were 165 reported suicides, which were fewer than the 220 predicted based on U.S. vital statistics data. However, because the degree of under-reporting of suicides is unknown, the fact that the reported number is lower than the predicted number cannot be interpreted as evidence against a causal association.

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